Summary

Rabies, a fatal and neglected zoonotic disease, is reported mainly from the southern parts of Bhutan bordering India, but sporadic occurrences have been reported in other, previously free areas. Domestic dogs play a principal role in the transmission of rabies and no wildlife rabies cases have been reported so far in Bhutan. Although rabies has been endemic and causes substantial financial losses, no detailed studies have been conducted to understand the epidemiology of rabies in Bhutan. The overall objective of this research was to better understand the epidemiology of animal and human rabies and estimate the cost of various rabies intervention measures in humans and animals. This was the first epidemiologic research on rabies ever conducted in Bhutan. Rabies surveillance data (1996 to 2009) and field surveys were used for this epidemiologic research.

The spatial and temporal distribution of animal rabies cases was examined by using a Geographic Information System and time series analysis approaches. The study showed that 59 of the 205 sub-districts in Bhutan reported animal rabies from 1996 to 2009 with increased incidences in the four districts in southern parts of Bhutan. Significant (P<0.05) clusters of cases were observed in south central and south west Bhutan. More cases were reported in cattle (n=447) and domestic dogs (n=317) and a significant cross correlation between the number of reported cases in dogs and other domestic animals was demonstrated, wherein the report of cases in dogs predicted cases in other domestic animals. Rabies cases were reported throughout the year with more reports during spring and summer months, likely to be associated with the breeding season of dogs. The annual patterns of cases were relatively stable until 2005, but increased in 2006 and 2008. This increased incidence was associated with re-emergence of rabies in eastern and south west Bhutan between 2005 and 2008, areas that had been previously free from rabies. This major rabies outbreak in eastern Bhutan resulted in one human and 256 domestic animal deaths while the outbreak in south west Bhutan resulted in 97 animal deaths; both outbreaks caused serious financial losses to society. During these outbreaks, large numbers of people (~2000) were directly or indirectly exposed to either suspected rabid animals or animal products derived from rabid animals and were given post-exposure prophylaxis. The outbreak in eastern Bhutan was believed to have been due to an
incursion from across the border while local spread from the endemic areas or an incursion was hypothesized in the south-west Bhutan outbreak. The high densities and movements of stray dogs with inadequate control measures were responsible for the rapid spread and persistence of the infection for about two years (from May 2005 to November 2007) in eastern Bhutan. In contrast, the outbreak in south west Bhutan during 2008 was controlled within six months by culling of stray dogs, mass dog vaccination, and impounding of dogs. Anthropogenic factors – including human population characteristics and its movement, road network accessibility, and high dog density – played a major role in the spread of disease during both of these outbreaks.

The assessment of risk factors for the occurrence of rabies at the sub-district level identified the socio-demographic and anthropogenic factors significantly associated with reporting of rabies in domestic animals in Bhutan. Sharing a common border with India was found to be the most important individual predictor of the overall distribution of rabies occurrence in Bhutan (odds ratio 10.43; 95% CI: 4.42–24.64; P<0.001). Of the 59 sub-districts that reported rabies in Bhutan, 43 (73%) shared a border with India. The trans-border movement or translocation of stray dogs and an inadequate control program may be responsible for the maintenance of rabies endemicity and transmission among the stray dog population in these border areas.

Molecular and phylogenetic analyses further demonstrated that Bhutanese rabies virus isolates were found to be closely related to Indian rabies virus strain and belong to Arctic-like-1 viruses which are widely circulating in the Indian sub-continent. This study suggests that the rabies viruses spreading in southern parts of Bhutan have originated from a common ancestor. However, more sampling is needed from Bhutan-India border areas to understand the transmission dynamic of rabies virus in the region.

In humans, rabies cases were found to be sporadic, mainly reported in the canine rabies endemic areas of southern Bhutan. A total of 15 human rabies deaths was reported between January 2006 and July 2011 (with 5 deaths reported in 2011 alone), equivalent to a cumulative incidence of 2.14 per 100000 population (annual incidence of 0.28 per 100000 people). Although the number of human rabies deaths was sporadic, there were increased number of dog bite incidents and post-exposure prophylaxis (PEP) administration to the patients. In order to understand the use and distribution of rabies
PEP in humans, PEP data for the period from 2005 to 2008 were retrieved from the hospital medical database and analysed. The study showed that PEP was provided to the patients free of charge by the medical hospitals in Bhutan, and followed the 5-dose Essen intramuscular regimen. A significant (P<0.001) difference in gender and age groups receiving PEP was observed: males received more PEP than females across all age groups. Children – particularly 5–9 years of age – received more PEP than other age groups, indicating children and males are more at risk of rabies exposure in Bhutan. PEP was provided throughout the year with a higher number of doses administered during the winter and spring months, and was given to both animal bite and non-bite exposures. The study also identified a lack of patient compliance to complete the course of PEP: some 40% (n = 3360) of the patients received an incomplete course of vaccine (less than the required course of 5-doses). However, the results suggest that patients with animal bite injury were less likely to receive an incomplete vaccine course than non-bite recipients. Secondly, patients presented to hospitals in rabies endemic or outbreak areas were less likely to receive an incomplete course than in rabies free interior Bhutan, thus reducing the chances of vaccination failures. The study also showed that the PEP was provided to patients that have low or no risk of rabies exposure. Therefore, a thorough assessment of each individual case based on the WHO guidelines would reduce unnecessary use of PEP, and therefore costs in Bhutan. The main reason for providing PEP was found to be due to dog bites.

To better understand the dog bites incidents in humans, a hospital-based survey was conducted at the three hospitals in Western and Southern Bhutan (Thimphu, Phuentsholing and Gelephu) for a period of nine months. The study revealed that dog bites in human are common in the survey areas and showed significant (P<0.001) gender and age differences in bite incidents. Males were more at risk of dog bites than females, and the children aged 5–9 years were bitten more than other age groups, which substantiate our earlier findings of more use of PEP in males and children. The majority of victims were bitten by stray dogs, and the most common anatomical bite sites were on the legs.

Using data on the anatomical location of dog bites in humans and a probability of dying from rabies, a decision tree model was constructed to estimate human deaths from rabies in two rabies endemic areas of southern Bhutan. Based on the official reported cases of
rabies in two hospital areas (Gelephu and Phuentsholing) in southern Bhutan, the average number of human rabies death was 1.5 (95% CI: 0.75–3.00) per year, equivalent to an annual incidence of 3.14 (95% CI: 1.57–6.29) per 100,000 population. The decision tree model predicted 2.23 (95% CI: 1.20–3.59) human deaths from rabies per year, equivalent to an annual incidence of 4.67 (95% CI: 2.53–7.53) deaths per 100,000 populations. This indicated that no major underreporting of human rabies deaths has occurred, unlike in other rabies endemic countries, although some underreporting of dog bites is possible. In the absence of post-exposure prophylaxis, the model predicted 19.24 (95% CI: 13.69–25.14) deaths per year, equivalent to an annual incidence of 40.31 (95% CI: 28.70–52.68) per 100,000 population, suggesting post-exposure prophylaxis is important to prevent human rabies deaths.

Since both dog bite incidents and the use of PEP were high in Bhutan, a cross-sectional study was conducted at Gelephu (south central Bhutan), an area endemic for rabies, to understand people’s level of knowledge and awareness about rabies. The study showed that a majority of the interviewed respondents had heard of rabies, and had a positive attitude towards the prevention and control of rabies. About 84 to 92% of the respondents also mentioned that they would report to the hospital for treatment if bitten by dogs and other animals, indicating good health seeking behaviours of the people. The respondents also had a positive attitude towards prevention and control of rabies in dogs by vaccination. However, these findings also indicated the existence of some knowledge gaps (knowledge about rabies and its transmission and importance of wound washing) which could be filled by creating awareness education programmes on: the danger of rabies and mode of transmission to humans and importance washing animal bite wound and visiting a hospital for post-exposure prophylaxis.

Since rabies causes substantial financial losses to society, understanding the cost-benefit or cost-effectiveness of the intervention programme is important. Quantification of the financial cost of rabies intervention in Bhutan suggested that the average direct medical cost of human PEP (using rabies vaccine only) was approximately Bhutanese Ngultrum (Nu) 1615 (US$ 35.65) per 5-dose Essen regimen per patient. The cost would increase to Nu. 2497 (US$ 55.13) and Nu. 19633 (US$ 433.41) per patient, if one dose of either equine rabies immunoglobulin (ERIG) or human rabies immunoglobulin (HRIG) was administered, respectively. The societal cost (public plus private cost) per patient was
estimated to be Nu. 2019 (US$ 45), Nu. 2901 (US$ 64), and Nu. 20037 (US$ 442) using vaccine alone, vaccine with ERIG and vaccine with HRIG, respectively. The average cost per dog vaccination was estimated to be Nu. 75 (US$ 1.66) and the cost per dog sterilization was estimated to be Nu. 288 (US$ 6.52). The total direct medical cost due to rabies (including surveillance and livestock loss cost, PEP in human and dog vaccination and sterilization) between 2001 and 2008 was estimated to be Nu. 48.54 million (US$ 1.07 million). The analysis also showed that mass dog vaccination would be more cost-effective than intensified post-exposure prophylaxis in human alone.

The above findings suggest that an area bordering India in the south were at higher risk of reporting rabies than the interior of Bhutan. More resources for rabies control programs and surveillance should be targeted and focussed in the highly endemic ‘hot spot’ areas of southern Bhutan. Mass vaccination of dogs in the border areas in the south would create an immune buffer (cordon sanitaire) and prevent incursion of rabies into interior Bhutan. A One-Health approach for rabies control in Bhutan should be implemented towards elimination of rabies through creation of effective partnership focussing on coordinating research, operational activities and pooling of resources between public health and veterinary services. Elimination of rabies through mass dog vaccination would reduce the recurrent cost of intensified PEP in humans and will produce economic savings in the long run by preventing human and livestock deaths and by discontinuing the intensified use of PEP in humans and rabies control programmes. Public awareness education is necessary and should include: the risk of rabies exposure; importance of preventing dog bites and wound washing and visiting health centres following dog bites and exposure to suspected rabid animals. Epidemiological surveillance of rabies should be improved by the laboratory confirmation of all suspected cases, including human, and the data so generated should be shared between the public health and veterinary sectors and also relevant international organizations. International collaboration is necessary for technical and financial support for sustaining rabies control in Bhutan.